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NIXON & VANDERHYE, PC
1100 N GLEBE ROAD
8TH FLOOR
ARLINGTON, VA 22201-4714

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,341	SHAW ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25, 31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 12/01/04 in response to the non-final Office Action mailed 07/01/04. With this, Applicants have amended the specification.

Status of Claims

2) New claims 31 and 32 have been added via the amendment filed 12/01/04.

Claims 1-23 and 25 have been amended via the amendment filed 12/01/04.

Claims 1-32 are pending.

Claims 1-25, 31 and 32 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraph 6(a) of the Office Action mailed 07/01/04 is withdrawn in light of Applicants' amendment to the specification.

6) The objection to the specification made in paragraph 6(b) of the Office Action mailed 07/01/04 is withdrawn in light of Applicants' amendments to the specification.

Specification - New Matter

7) The instant specification is objected to for the following reasons:

(A) The paragraph inserted at line 16 of page 6 of the specification via the amendment filed 12/01/04 is objected to under 35 U.S.C. § 132, because it appears to introduce new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The recitations: 'Figure 1 shows induction .....receiving buffer alone'

is new matter. Applicants have not pointed to specific parts of the specification, as originally filed, for the newly added paragraph.

(B) The limitation in claims 3 and 4: 'heterologous antigen ... induce... immunogenicity against a pathogenic microorganism' is new matter, because the specification does not support such a limitation. Similarly, the limitation in claims 5 and 9: 'heterologous antigen ... induce... immunogenicity against a pathogenic organism' is new matter, because the specification does not support such a limitation.

Rejection(s) Withdrawn

8) The rejection of claims 16, 18, 19, 23 and 25 made in paragraph 7 of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, first paragraph, as being non-enabled, with regard to the deposit issue, is withdrawn in light of Applicants' arguments. Applicants cite prior art reference(s) and state that *Lactobacillus plantarum* 256 was available in the art to skilled artisans.

9) The rejection of claim 1 made in paragraph 9(a) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of claims 2-17 made in paragraph 9(b) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

11) The rejection of claim 2 made in paragraph 9(c) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claims 3 and 15 made in paragraph 9(d) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

13) The rejection of claims 5 and 6 made in paragraph 9(e) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

14) The rejection of claim 5 made in paragraph 9(f) of the Office Action mailed 07/01/04

under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claim 5 made in paragraph 9(h) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

16) The rejection of claim 7 made in paragraph 9(i) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claim 5 made in paragraph 9(j) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

18) The rejection of claim 9 made in paragraph 9(k) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

19) The rejection of claim 11 made in paragraph 9(l) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

20) The rejection of claim 18 made in paragraph 9(m) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

21) The rejection of claim 23 made in paragraph 9(n) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

22) The rejection of claim 15 made in paragraph 9(o) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

23) The rejection of claims 19, 21 and 25 made in paragraph 9(q) of the Office Action mailed

07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

24) The rejection of claim 21 made in paragraph 9(r) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

25) The rejection of claim 22 made in paragraph 9(s) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

26) The rejection of claims 2-19, 21, 23 and 25 made in paragraph 9(t) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

27) The rejection of claim 21 made in paragraph 12 of the Office Action mailed 07/01/04 under 35 U.S.C. § 102(b) as being anticipated by Mercenier *et al.* (*Adv. Food Sci.* 18: 73-77, 1996), is withdrawn in light of Applicants' amendment to the claim.

28) The rejection of claims 1 and 8 made in paragraph 14 of the Office Action mailed 07/01/04 under 35 U.S.C. § 103(a) as being unpatentable over Pouwels *et al.* (*Int. J. Food Microbiol.* 41: 155-167, May 1998 - Applicants' IDS) in view of Claassen *et al.* (*In*: *Recombinant and Synthetic Vaccines*. (Ed) Talwar GP *et al.* Narosa Publishing House, New Delhi, 407-412, 1994) and Wells *et al.* (*Antonie van Lewuwenhoek* 70: 317-330, 1996 - Applicants' IDS) (Wells *et al.*, 1996), is withdrawn. The claims are rejected below under 35 U.S.C. § 102.

Rejection(s) Maintained

29) The rejection of claim 5 made in paragraph 9(g) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

Applicants state that they have amended claim 5 to recite 'pathogenic organism' to render the issue of whether or not *Pneumocystis pneumonia* is a microorganism moot. Applicants further submit that *Pneumocystis pneumonia* is a pathogenic organism regardless of whether or not it is a microorganism.

Applicants' arguments have been carefully considered, but are not persuasive. The names of microorganisms are usually indicated in art by italicized terminologies. It is still not clear whether the italicized term '*Pneumocystis pneumonia*' represents a pathogenic microorganism or a clinical condition caused by a eukaryotic parasite. The art recognizes either the pathogenic microorganism '*Pneumocystis carinii*' or a clinical condition 'pneumonia' caused by '*Pneumocystis carinii*'. What exactly is encompassed in the instant limitation '*Pneumocystis pneumonia*' is not clear. The rejection stands.

30) The rejection of claim 16 (not claim 15 as mistyped) made in paragraph 9(p) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

Applicants state that claim 16 has been amended to specify that the *Lactobacillus plantarum* 'is recombinant *Lactobacillus plantarum*'. However, it does not appear that such an amendment has indeed been made. The rejection stands.

31) The rejection of claims 1-7 and 9-25 made in paragraph 11 of the Office Action mailed 07/01/04 under 35 U.S.C. § 102(b) as being anticipated by Pouwels *et al.* (*J. Biotechnol.* 44: 183-192, 1996) (Pouwels *et al.*, 1996) as evidenced by Hoshino *et al.* (*J. Virol.* 62: 744-748, 1988, abstract) or Virelizier JL (*J. Immunol.* 115: 434-439, 1975, abstract), Naidu (US 20020192202 A1) and Wells *et al.* (*Antonie van Lewuwenhoek* 70: 317-330, 1996 - Applicants' IDS) (Wells *et al.*, 1996), is maintained for reasons set forth therein and herebelow.

Claims 31 and 32 are now added to this rejection, since Pouwels' (1996) vaccine is usable for administration to a human, including a normally healthy adult and since Pouwels' heterologous antigen is from influenza virus which enters the body mucosally.

Applicants contend that Pouwels *et al.* (1996) do not disclose an oral vaccine comprising a *Lactobacillus plantarum* strain modified to express a heterologous antigen where the bacterium is capable of eliciting an immune response against the antigen or indeed any *Lactobacillus* bacterium capable of eliciting such a response. Applicants refer to a passage from section 3.5 on page 189 of Pouwels *et al.* (1996) and state that administration in Pouwels *et al.* (1996) is first subcutaneous and then oral, and that there is no indication that the bacterium can act as an oral vaccine. Applicants further allege that there is no indication that *Lactobacillus plantarum* was administered orally since

the section only refers to administering "*Lactobacillus*" without mentioning a 'genus' for the bacterium. Applicants argue that it is perfectly possible that the administered bacterium was *Lactobacillus caseii*. With this, Applicants assert that a generic disclosure cannot anticipate a specific element. Applicants assert that there is no indication that any of the *Lactobacillus* strains discussed are able to generate an immune response against the antigen when administered orally, and that indeed the strains referred to may well not do so. Applicants state that the oral administration of the bacterium in Pouwels *et al.* (1996) is being used as a 'booster' and not as an oral vaccine. Applicants state that oral boosting following subcutaneous administration and oral vaccination are very different things. Applicants discuss the chief advantages of oral vaccination in that it is a quick, painless and cheap administration route. Applicants state that the "boosting" effect seen in Pouwels *et al.* (1996) cannot be said to be an oral vaccination and that there is no evidence that any of the strains discussed in Pouwels *et al.* (1996) could give rise to successful oral vaccination.

With regard to the evidentiary citations provided by the Office, Applicants submit that immunogenicity is not just a question of the proteins employed, but is very much a question of the context in which the protein is administered. Applicants state that a protein may give rise to an immune response when administered in a particular route or context, but fail to do so when it is administered via a different route or context. Applicants state that administering a protein alone may not generate an immune response, but a protein presented on the surface of an *L. plantarum* as in the invention can. Applicants further assert that one needs to select the correct administration method, type of bacterial strain, and antigen presentation in order to be successful.

Applicants' arguments have been carefully considered, but are non-persuasive. The reference of Pouwels *et al.* (1996) is properly applied as an anticipatory prior art. The term 'oral vaccine' is specifically defined within the instant specification. For example, lines 19 and 20 of page 7 of the instant specification states that 'oral vaccine' means any vaccine suited, adapted, intended and/or formulated for oral delivery. The prior art vaccine meets this definition. In fact, the prior art vaccine was administered orally to mice following which a significant immune response to the HA beta-glucuronidase heterologous protein was observed (see section 3.5). Contrary to Applicants' speculation that what was administered orally could have been *L. casei*, from Pouwels's (1996) disclosure it appears that all of the four '*Lactobacillus* transformants' including the three *L.*

plantarum species expressing the HA-*uidA* gene have been administered to mice. *Arguendo*, even if one believes that all four transformants were not orally administered, it is clear from section 3.5 of Pouwels *et al.* (1996) that what were orally administered were the *Lactobacillus* transformants harboring the HA-*uidA* gene that 'were cultivated for 7 h', which induced a significant booster serum immune response in mice. From Figure 4 depicted above the section 3.5, one can readily see that the *Lactobacillus* transformant that was cultivated for 7 h is 'L.p. 14917'. 'L.p. 14917' is described in section 3.4 as '*L. plantarum* ATCC 14917' encoding the Hackett epitope of the influenza virus haemagglutinin fused with beta-glucuronidase. It is important to note that the limitation 'immune response', for instance in claim 1, encompasses any immune response including booster immune response or serum immune response. Claim 1 does not specifically recite in whom the immune response is elicited. The bacterium recited in claim 1 is only required to be 'capable' of expressing a heterologous antigen. The limitation in claim 1, 'can elicit an immune response', indicates that the elicitation of an immune response against the heterologous antigen is optional, but not a requirement. Whether or not the oral administration of the Pouwels (1996) vaccine was preceded by a subcutaneous administration is not relevant since the instant claims are not drawn to a method of administration of the vaccine that is exclusively oral. Instead, the claims are drawn to a product that is intended to be administered orally, or is formulated for oral delivery as defined by Applicants at lines 19 and 20 of page 7 of the specification. With this definition of the 'oral vaccine', Pouwels *et al.* (1996) do not even have to teach that their vaccine was orally administered. The vaccine claimed in instant claim 1 is only required to be intended for oral administration and is required to elicit an immune response irrespective of what the route of administration is. The Pouwels (1996) vaccine meets the structural elements of the instantly claimed vaccine, including the one claimed in claims 18 and 20-2; and it also meets the functional limitations. For the reasons delineated above, the rejection stands.

32) The rejection of claims 20 and 22 made in paragraph 12 of the Office Action mailed 07/01/04 under 35 U.S.C. § 102(b) as being anticipated by Mercenier *et al.* (*Adv. Food Sci.* 18: 73-77, 1996), is maintained for reasons set forth therein and herebelow.

Applicants acknowledge that Mercenier's *Lactobacillus* bacterium modified to express M6 protein elicits an immune response to the M6 protein. Applicants argue that the immune response

was not raised against the antigen fused to the M6 protein. Applicants contend that section 2.3 of Mercenier refers to a non-human recombinant *Lactobacillus paracasei* strain expressing the antigens V3 or gp41 E protein wherein the antigens are fused to sequences encoding the M6 carrier protein and that no immune response against either antigen was raised. Applicants further submit the following statement:

> A strain for use in an oral vaccine is not of much use if it is unable to elicit an immune response against a chosen antigen as specified by the claims!

Applicants' arguments have been carefully considered, but are non-persuasive. The M6 protein of *Streptococcus gordonii* expressed intracellularly or on the surface by Mercenier's recombinant *Lactobacillus* bacterium qualifies as a heterologous protein antigen, against which an immune response was elicited in mice on oral immunization (see pages 74 and 75; and Figure 1). The recombinant *Lactobacillus casei* strain persisted in the intestine for 6-8 days (see page 76 and Table 1). Thus, Mercenier's recombinant *Lactobacillus* bacterium was indeed able to elicit an immune response against the heterologous M6 antigen on oral administration to mice and therefore served as an efficient oral vaccine. The rejection stands.

33) The rejection of claim 16 (not claim 15 as mistyped) made in paragraph 9(p) of the Office Action mailed 07/01/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

Applicants state that claim 16 has been amended to specify that the *Lactobacillus plantarum* 'is recombinant *Lactobacillus plantarum*'. However, it does not appear that such an amendment has indeed been made. The rejection stands.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

34) Claims 5 and 9 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The added limitation: 'organism' in claims 5 and 9 is new matter. The limitations: 'heterologous antigen ... induce... immunogenicity against a pathogenic organism' constitute new matter, because there appears to be no descriptive support in the specification, as originally filed, for

these limitations. Therefore, the above-identified limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

35) Claims 1-25, 31 and 32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 1 is vague and indefinite in the limitation: 'can elicit an immune response against the heterologous antigen', because it is unclear in whom could the immune response be elicited by the bacterium. Does the limitation 'can elicit an immune response' indicate that elicitation of an immune response is optional?

(b) Analogous criticism applies to claims 9 and 18.

(c) Claims 3-5 are vague and confusing in the recitation 'induce.. immunogenicity against a pathogenic .....organism', because it is unclear what exactly does this mean. The term 'immunogenicity' represents a property of an antigen. It is unclear how an antigen can induce a property of an antigen against a pathogenic microorganism. Do Applicants mean to recite 'immune response' as in the amended claim 1?

(d) Claims 1, 2 and 18 are confusing and/or lack clarity in the limitations 'capable' (see line 2). Does the limitation 'capable' indicate that the claimed bacterium may or may not express a heterologous antigen?

(e) Claim 18 is vague and indefinite in the use of the limitation: 'optionally' because it is unclear what kind of limiting effect does this recitation has on the subject matter or scope of the claim.

(f) Claims 2, 3, 7, 12-13 and 18 include recitations such as 'optionally', 'suitably' and/or 'preferably', which render the claims indefinite, because it is unclear in what way these recitations

limit the subject matter of the claims.

(g) Claim 14 is vague and indefinite in the limitation: 'equivalent conditions' because it is unclear which conditions qualify as equivalent conditions. How long *L. plantarum* 80 or NCIMB8826 persists in an individual, vaccinated or not, is not disclosed. Since under which precise conditions *L. plantarum* 80 and NCIMB 8826 persisted is not disclosed, what conditions qualify as 'equivalent conditions' is not clear.

(h) Claim 9 has improper antecedence in the limitation: 'the pathogenic organism'. Claim 9 depends from claim 1, which does not recite 'a pathogenic organism'.

(i) Claim 11 is vague, indefinite and confusing in the comparative language: 'a degree exceeding that of *Lactobacillus plantarum* 80 ..'. In the absence of a recitation disclosing the exact level of expression of beta-galactosidase by *Lactobacillus plantarum* 80, the level of expression of the heterologous antigen by the claimed recombinant *Lactobacillus plantarum* cannot be envisaged.

(j) Analogous criticism applies to claim 14 with regard to the comparative language: 'a persistence longer than that of *L. plantarum* 80'.

(k) Claim 20 is vague, indefinite and confusing in the limitation: 'non-human .... *Lactobacillus* bacterium', because it is unclear what Applicants are trying to convey. Is the term 'non-human' referring to the source of the recited bacterium?

(l) Claim 20 is further vague and indefinite in the limitation: 'modified', because it is unclear what is encompassed in this limitation. What process has to be carried out that qualifies as 'modification' and how the process of modification changes the structure of the claimed bacterium structurally is not clear.

(m) Claim 21 is vague, indefinite and confusing in the limitation: 'The bacterium according to claim 20 wherein ..... the bacterium is a naturally occurring or unmodified *L. plantarum*'. Claim 21 depends from claim 20 which recites that the *Lactobacillus* bacterium 'has been modified'. It is unclear how the 'modified' bacterium of claim 20 can become an 'unmodified' *L. plantarum* in the dependent claim 21.

(n) Claim 24 includes limitations within brackets: '(on a cell surface)' and raises an indefiniteness issue as to whether or not the recited feature is optional.

(o) The limitation 'pathogenic organism' in claims 5 and 9 is inconsistent, with regard to

the scope, with the limitation: 'pathogenic microorganism' in claims 3 and 4. The above-identified two limitations are further inconsistent in scope with the limitation 'pathogen' in claims 3 and 31.

(p) Claim 5 is redundant in the duplicative limitations: 'species of the genus *Clostridium perfringens*'.

(q) Claim 13 has improper antecedence in the limitation: 'claim 1 wherein the recombinant *Lactobacillus plantarum* strain'. Claim 13 depends from claim 1, which does not recite any such 'strain'.

(r) Claim 13 is further vague and indefinite in the limitation: persistence in a vaccinated individual'. It is unclear what is this individual vaccinated with.

(s) Claim 18 has improper antecedent basis in the limitation: 'the bacterium' (see lines 4 and 5), because there is no earlier recitation of any 'bacterium' in the claim.

(t) Claim 19 has improper antecedent basis in the limitation: 'The bacterium according to claim 18', because claim 18 is drawn to a 'recombinant *Lactobacillus plantarum*', but does not recite a 'bacterium'.

(u) Claim 22 is vague in the limitation: 'that individual' (see last line). For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the limitation with --said individual--.

(v) Claim 23 lacks proper antecedence in the limitation: 'A *Lactobacillus plantarum* according to claim 18'. For proper antecedence, it is suggested that Applicants replace the limitation with --The *Lactobacillus plantarum* according to claim 18--.

(w) Claims 2-17, 31 and 32, which depend directly or indirectly from claim 1, are also rejected as being vague and indefinite because of the indefiniteness identified above in the base claim.

(x) Claims 19, 23 and 25, which depend directly or indirectly from claim 18, are also rejected as being vague and indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

36) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

37) Claims 1 and 8 are rejected under 35 U.S.C. § 102(a) as being anticipated by Maassen (*J. Immunol. Methods* 223: 131-136, February 1999, already of record).

Maassen taught that she/he developed genetically engineered lactobacilli as oral vaccines wherein recombinant lactobacilli express microbial heterologous antigens on the cell surface and induce antibodies in mice on oral administration (see page 131; section 2.3; and page 135). One such product was a recombinant *Lactobacillus plantarum* 256 transformed with a plasmid encoding tetanus toxin fragment C, pLP401-TTFC (see section 3.5).

Claims 1 and 8 are anticipated by Maassen.

38) Claims 1-6, 9-12, 14, 15, 20, 21, 24, 31 and 32 are rejected under 35 U.S.C. § 102(b) as being anticipated by Madsen *et al.* (WO 98/10079).

Madsen *et al.* disclosed recombinant lactic acid bacterial cells containing a gene expression system expressing a pharmaceutically or immunologically active polypeptide(s) from *M. tuberculosis* (i.e., a heterologous antigen) wherein the recombinant bacterial cells are useful as food, i.e., for oral consumption, feed starter cultures, or vaccines, or as animal feed (see abstract; last paragraph on page 7; first half of page 8; and paragraph bridging pages 17 and 18 and paragraph bridging 18 and 19). The recombinant lactic acid bacterium used is *Lactobacillus plantarum* (see last full paragraph on page 16). An expression system having the *lac* promoter and being able to express tetanus toxin fragment C is taught (see first full paragraph on page 4). The biologically functional gene expressed via the recombinant lactic acid bacterium is a toxin, enzyme, microbial cell surface protein, or a viral capsid protein (see first full paragraph on page 13). The recombinant bacteria express on their outer surface or intracellularly an immunologically active gene product(s) comprising at least one epitope from any pathogenic organism against which there is a need to immunize an animal, mammal or human being. Such a product is used as a vaccine (see pages 14 and 15). The recombinant bacterium expressing a heterologous gene product is administered as improved food (i.e., orally administered product) (see paragraph bridging pages 18 and 19). The immunologically active gene product expressed via the recombinant lactic acid bacterium usable as a vaccine composition is an antigen such as *M. tuberculosis* MPT64 antigen or ESAT-6 polypeptide, an epitope, a polypeptide comprising an epitope, or an antibody (see last two full paragraphs on page 20). The lactic acid

bacteria used in recombination are isolated from mammals, human beings, birds or fish (see paragraph bridging pages 19 and 20).

Claims 1-6, 9-12, 14, 15, 20, 21, 24, 31 and 32 are anticipated by Madsen *et al.*

Objection(s)

39) Claim 6 is objected to for the incorrect non-italicized format of the limitation: 'Mycobacterium tuberculosis'. To be consistent with the practice in the art and with the correct format in claim 5, it is suggested that Applicants replace the limitation with --*Mycobacterium tuberculosis*--.

Remarks

40) Claims 1-25, 31 and 32 stand rejected.

41) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

42) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free)..

43) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

February, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER